Reviewer's report

Title: Patterns of Use, Dosing, and Economic Impact of Biologic Agent Use in Patients with Rheumatoid Arthritis: A Retrospective Cohort Study

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Reviewer: mark nuijten

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This is in general a solid study, which shows the real costs in daily practice of biologicals. This is especially relevant because of the high annual drug costs. It appears that biologicals are not used according to the label, and that actual costs are higher because of dose increase. The analysis shows that especially Remicade is used in higher dosage, which was found also in other studies. I recommend the authors including these references in the conclusion, because it strengthens their findings for Remicade.

With regards to Enbrel, there are no studies, which show a dose increase. Therefore the small increase of Enbrel in this study should be considered with prudence, but further research is required.

References:

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For example, a patient initially receiving infliximab and later receiving etanercept would be classified as an “infliximab” patient for the duration of the study period.

This approach seems to be based on intention to treat, which is often ideal approach for cost-effectiveness studies. However, in this case the objective of the study is to assess the real costs associated with biologics in real practice compared with labeling information. The current approach is not suitable for calculation of this differences, when the Remicade analysis contains Enbrel patients and the Enbrel analysis contains Remicade patients. The current design compares first-choice treatment with Remicade with first choice treatment with Enbrel.

Another pitfall may be that patients may increase the dose in case of lack of efficacy. However, lack of efficacy may also lead to a switch to another biological. The current analysis does not consider this option.

Page 7: Infliximab and etanercept doses reported at the third infusion/prescription respectively were considered to be the maintenance dose levels.

There may have been already dose escalation during the initial start of the treatment. In this case maintenance treatment may already be higher than according to the label. I would recommend a table showing how many % of patients at the start of maintenance treatment have a dose, which is higher than the label.

Page 9: regression model should ideally contain a measure of severity of RA. However, the data base probably does not contain clinical measures of severity. Another important variable may be working status of the patient. Authors may address these variables, and explain, why these variables
were not included.

Page 10: Most patients in the sample were members of an HMO or PPO product; however, the use of infliximab was much lower in the HMO group compared to etanercept (30% vs. 45% respectively) and substantially higher among PPO patients (49% vs. 35% respectively).

Is there an explanation for this remarkable result, when considering financial systems between HMO and PPO?

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Therefore, these results may not reflect the true amount of infliximab utilized and may in fact understate the rate of dose escalation, as a patient who increases from 1.2 to 1.7 vials will be shown to have utilized 2 vials in both instances.

This may indeed underestimate real use, especially for patients with a weight just over 70 kg, who just have to use 3 vials. They need 2,1 vial, but have to increase to 3,1 vials in order to need an extra vial. Consequently a lot dose increases are masked. Authors may add estimation for this effect.